Remarks and Response

Applicant appreciates the Examiner's apparent withdrawal of the prior rejection of the claims under 35 U.S.C. §101 and of claims 250, 256 or 257 under 35 U.S.C. §103(a) over Leet (US Pat. No. 6,000,828), in further view of Rivette (US Pat. No. 5, 991,751), since no rejection on either basis is reiterated in the present Action.

Applicant has corrected one obvious typographical error in the specification at paragraph [00040], for which no additional support is needed. Amendments made in response to the Examiner's comments in the Office Action, and support will be addressed below in the relevant arguments. The addition of the term "previously unreported" in place of "novel" before essential adverse event" in claims 250, 270, 271, 278, 280, 281, 282, 285, 286 and 296 is supported, at least, by paragraph [0040]. The addition of the "wherein" clause in claim 250 is supported, at least, for example, at paragraph [0070] regarding the restricted use and providing the warning, and at paragraph [0071] regarding providing instructions for the new use. Neither new claims nor new matter has been added.

Response to the Rejection under 35 U.S.C. §112, first paragraph

The Examiner has rejected Applicant's pending claims 250, 285, and 298 under 35 U.S.C. §112, first paragraph as failing to comply with the written description requirement. In making this rejection the Examiner has pointed to specific phrases that are problematic to his examination.

In claim 250, the Examiner argues that neither the phrase "novel essential adverse event," nor "novel method of use" is described in the specification. Presumably it is the term "novel" that the Examiner finds objectionable, although Applicant cannot be certain of the Examiner's basis for the rejection since no further explanation is given. The basis for "essential adverse event" was fully argued by Applicant in the Response to the previous Office Action, so there can be no question about the meaning of that term. Support may be found at least at paragraphs [0011], [0040], [0042], [0048], [0051], [0056], [0070], [0072],[0076], [0077], [0079], [0085], [0087], and [0095]-[0098]. The basis for "method of use" is a recognized term of art. As a result, the rejection can only be found in Applicant's use of the word "novel." Accordingly, in light of Applicant's

current amendment to the claim, the rejection is moot, and Applicant asks that it be withdrawn.

In an effort to assist the Examiner's understanding of Applicant's invention, Applicant has further added a "wherein" clause limiting the claimed method of use in claim 250 to the choices provided in the Markush group. Support for this addition is provided above, and in light of this addition, Applicant's claimed method of use is more fully defined.

In claim 285, the Examiner argues that the term "chronic immune mediated disorder" lacks support in the specification. However, if the Examiner returns to the application as filed (also Patent Publication 2002/0083080), the subject phrase is found in original claims 30, 68, 138, and 194, each of which contain the phrase "wherein the at least one new essential adverse event is based upon neither a drug interaction, nor a chronic immune mediated disorder." Since the original claims do, in fact, form a portion of the specification, and are sufficient to support subsequent claims – the phrase "chronic immune mediated disorder" is completely supported by Applicant's specification.

As shown in Applicant's use of the phrase, a "chronic immune mediated disorder" is defined as an unnecessary adverse event. Consequently, in order to provide support in the present body of the specification based upon the use in the original filing, if the Examiner will agree, Applicant is willing to amend the definition of an unnecessary adverse event in paragraph [00095] as follows:

> [0095] An 'unnecessary adverse event' would be an essential adverse event that could be or could have been easily avoided. One example would be a drug interaction, which could be avoided by withholding one of the interacting drugs, or a chronic immune mediated disorder. Another example of an unnecessary adverse event is one in which the adverse event can be or could have been avoided by using a different product, or even a different brand. For example, if a drug is very toxic in a subgroup of people, *e.g.*, people of a certain age, or those who have a preexisting condition, then the adverse event in such individuals groups can be or could have been easily avoided by using a different drug or different treatment, for example, surgery.

Applicant believes that this amendment will render the rejection moot, but first asks the Examiner whether such an amendment will be permitted.

In claim 298, the Examiner argues that the term "new dosing regimen" lacks support in the specification. However, contrary to the Examiner's argument, the phrase is

supported, at least, the last sentence of paragraph [0036], which reads: "Preferably, the adverse event (or new use) is one other than one related to dosing including the timing of dosing (or optimizing dosing)." This clearly defines what one skilled in the art would obviously recognize as a "new dosing regimen," when as required a meaning is assigned to the term in Applicant's claims, "taking into account the entire disclosure." Applicant has introduced neither unconventional terminologies under MPEP 7.01, nor new matter.

The law is clear that the invention need not be described in exactly the same words in the specification and the claims. See, *e.g.*, *Purdue Pharma, L.P. v. F.H. Faulding & Co.*, 48 F. Supp. 2d 420, 426-27 (D. Del. 1999) (stating that claimed subject matter need not be described in *hoc verba* in the patent specification, but that it must be claimed in such a way as to show that the inventor was in possession of the invention when the application was filed). See also *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997) (explaining that for the inventor to show that he is in possession of the invention, he must describe the invention with all of its limitations, not just enough to make what is claimed obvious based on the disclosure); *In re Wilder*, 736 F.2d 1516, 1520 (Fed. Cir. 1984) (stating that the subject matter need not be described in an identical manner and that the degree to which the original description must correspond to the claims in order to meet the written description requirement must be decided on a case-by-case basis).

Thus, it is the ability of the phrase to show that Applicant was in possession of his invention and the meaning of the phrase as supported by the specification that is intended by the patent laws, not whether the phrase in the claim is found *ipsis verbis* in the specification. From the specification as a whole, there can be little doubt that Applicant was in full possession of the invention set forth in claim 298, including the reference made to "new dosage regimen." As used in the claim statement "[t]he proprietary method of use of claim 250, wherein the use is one other than a new dosing regimen" the subject phrase is supported by Applicant's statement in paragraph [0036]. In that paragraph Applicant defines what is referred to by the term "adverse event" and then at the end of the paragraph states that an adverse event "is other than dosage," more specifically other than the "timing of dosing (or optimizing dosing)," which is commonly known in the art to be a dosage regimen.

Accordingly, it is argues that the rejection with regard to Applicant's phrase in claim 298 is misplaces, and Applicant respectfully asks for reconsideration and withdrawal of that rejection.

Response to the Rejection under 35 U.S.C. §112, second paragraph

The Examiner has rejected Applicant's claims 280 and 293 under 35 U.S.C. §112, second paragraph as failing to point out and distinctly claim that which Applicant regards to be the invention. In making this rejection the Examiner states that the claims are indefinite because of the multiple appearances of the word "or" in each claim. In light of the amendments attached hereto to claims 280 and 293, the rejection under 35 U.S.C. 112, second paragraph, is moot. Accordingly, Applicant, therefore, respectfully asks that the rejection be withdrawn.

Response to the Rejection under 35 U.S.C. §112, first and second paragraphs

The Examiner has rejected Applicant's claims 285, 286, and 298 under 35 U.S.C. §112, first paragraph as indefinite; and claims 280 and 293 under 35 U.S.C. §112, second paragraph as failing to point out and distinctly claim that which Applicant regards to be the invention. In making this rejection the Examiner states that the claims are in such condition that he is unable to understand the present invention, and that as a result no art rejection is possible.

In response, Applicant points out that the subject claims have been amended or explained, to the extent that it is believed the Examiner can understand the subject matter being claimed. This rejection is moot, and it is requested that it be withdrawn.

Response to the Rejection under 35 U.S.C. §103(a)

Regarding ADPA, Stanton and Rivette:

The Examiner has rejected Applicant's claims 250, 256, 257, 270-276, 278, 281-282, 287-290, 292, and 294-297 under 35 U.S.C. §103(a), as obvious and unpatentable over applicant disclosed prior art (ADPA) in view of Stanton (US Pub. No. 2002/0039990), in further view of Rivette (US Pat. No. 5, 991,751). In making this rejection the Examiner refers to ADPA as found in paragraph [0050]. Applicant has no way of knowing which specific "prior art" the Examiner is referring to, but did find that paragraph [0050] refers to "Sources of prior known essential adverse events can include

package inserts, the Physician's Desk Reference, The Merck Manual, data from regulatory agencies such as the FDA, and published literature found on databases such as MEDLINE." Applicant does NOT admit that such statement or any statement in paragraph [0050] identifies "prior art" to the presently claimed invention. Applicant admits only the he has identified "sources of prior known essential adverse events" – but this is not the subject matter claimed in Applicant's invention. Consequently, no admission of the type referred to by the Examiner has been made by Applicant, and no admission has been made as to any prior art as to the subject matter actually claimed by Applicant to define his invention. Accordingly, Applicant asks for a withdrawal by the Examiner that suggests that Applicant has admitted to disclosing any prior art of any kind with regard to Applicant's claimed invention.

Nevertheless, Applicant will address the cited references combined with the ADPA. The Stanton publication specifically underlies all of the Examiner's patentability rejections. However, Stanton was published April 4, 2002 (almost 1 year after effective filing date (February 22, 2001) of Applicant's U.S. Provisional Application No. 60/270,697). As such, all the rejections based on Stanton as the underlying reference must fail, as being based on an improper prior art reference.

Even if that were not true, Stanton must still fail as a prior art reference against Applicant's invention. Regarding the Examiner's arguments Stanton in view of Rivette, Stanton's publication relates expressly to genetic screening (see title "Gene Sequence Variances in Genes Related to Folate Metabolism having Utility in Determining the Treatment of Disease"). The Stanton abstract specifies "Methods of determining relevant variance information and additional methods of using such variance information are also described." The specifications in particular mentions defines the invention as relating expressly to "pharmacogenetic studies" see, *e.g.*, paragraphs 6, 124, 136, 157, 194,195, 196, 197, 297, 300, 301, 302,303,305-311, 312, 314-318, 327, etc. Thus, in Stanton's own words, his invention is based on pharmacogenics. See Stanton paragraph [0157]:

> [0157] Practice of this invention will often begin with identification of a specific pharmaceutical product, for example a drug, that would benefit from improved efficacy or reduced toxicity or both, and the recognition that pharmacogenetic investigations as described herein provide a basis for achieving such improved characteristics.

By contrast, Applicant's invention *expressly* excludes pharmogenetics/ pharmacogenomics. The terms can be used interchangeably. See Applicant's specification at paragraph [0103]:

> [0103] Nevertheless, the present invention is not intended to encompass pharmacogenomic techniques for screening.

A description of this difference can be found in Applicant's earlier patent (See, US patent 6,584,472 (Classen) at column 5, paragraph 3) which is included by reference and cited in the present application (see Applicant's present application at paragraph [0003] referencing U.S. Ser. No. 09/804,289). See also the disclaimers (Classen application, paragraphs [0114], [0115]), which include the cited Classen patent and teachings by reference.

The cited paragraph in the Classen '472 patent states at col. 5, para 3 that:

> Pharmacogenetics and pharmacogenomics are fields dedicated to determining the genetic basis for pharmaceutical phenomenon, such as drug metabolism. For example pharmacogenetics has been utilized to determine why some individuals metabolized a drug faster than another. This approach has been successful when a single enzyme is responsible for the event. Pharmacogenomics is similar to pharmacogenetics, but involves studying the effects of multiple different genes on a characteristic, such as drug metabolism or adverse event. The goal of these fields is to develop genetic tests to individualize pharmaceutical treatment based on a person's genes. However, these fields do not involve screening databases for new adverse events, rather they start with a defined adverse event, and then attempt to determine the molecular cause of the event. If the pharmacogenetic study leads to a new use, that use involves the use of specific laboratory test, usually a molecular test, in conjunction with the administration of the selected drug. In this situation a prospective clinical trial is needed before regulatory approval, *i.e.*, FDA approval, of the new use. Thus, the new use is not the result of the discovery of the adverse event; it is the product of the clinical trial.

Applicant's exclusion of pharmacogenomics/genetics was not simply to exclude prior art, but because the methods are distinctly different - as clearly seen between the teachings of Classen and Stanton.

Moreover, Stanton fails to make any reference of any kind to an adverse event as being either "new" or "essential." Further, the Stanton claimed method of use is not "responsive" to identifying a new or previously-unreported, essential adverse event; rather it refers only to a clinical trial program. At paragraph 293-297, Stanton states, *e.g.*, that a clinical trial is needed to test the "therapeutic invention" (Stanton paragraph 296). This is to be expected and remains consistent with the definition of pharmacogenomics with regard to the Stanton invention.

In marked contrast, according to Applicant's invention there is *no clinical trial required*, nor does such a trial provide the necessary warning(s). Furthermore if a clinical trial were needed to obtain regulatory agency approval, as is the case with Stanton's published application, *then the resulting data is not "essential" since a regulatory body does not require that the information be made public*, because public access is permitted to the findings **only** if there is sufficient clinical trial data supporting its use. Thus, the Stanton method of using the information is not comparable to Applicant's claimed method of use because Stanton's method is NOT "responsive" to discovering a previously-unreported essential adverse event but the result of a clinical trial program. The Stanton invention comprises a kit containing at least one probe (Stanton paragraph [0075]). This requires use in the clinical trial of a probe "approved by a regulatory agency." By contrast, kits described by Applicant (see paragraph [0079]) which provide warnings – DO NOT require regulatory approval.

Stanton teaches that the inventive "process of 'identifying' or discovering new variances involves comparing the [nucleotide] sequence of at least two alleles of a gene." (Stanton , paragraph [0035]). Again this refers to expressly to pharmacogenetics. Furthermore Stanton states at paragraph [0036] that "The process of determining involves using diagnostic tests for specific variances or variant forms of gene (genes)." This again refers to pharmacogenetics. By contrast, however, although Stanton at paragraph [0019] and [0114] refers to "adverse events," Stanton never states or even suggests that the adverse event is "essential" as defined by Applicant, nor that it is "new" or "novel" or "previously unreported" or unknown – as would be required of an inventor conceiving of a proprietary invention. Consequently, Stanton makes no requirement that the "adverse event" MUST be "new" or "novel" or "previously unreported" or unknown.

What is patentable in Stanton's publication, if anything is patentable, is only the information about the gene variance and the "old" or "known" or "previously reported" adverse event. Stanton lists adverse events at paragraph [0017], including nausea, weakness, dizziness, diarrhea, but Stanton does not claim these adverse events are themselves "new," nor does Stanton's invention require that they be new. These types of adverse events were likely reported at an early stage for all drugs.

In fact, the difference between Applicant's requirement that the essential adverse events must be "previously unreported" (meaning novel) and Stanton's use of known information becomes abundantly clear in Stanton's paragraph [0053], where Stanton expressly admits that "the variance may be *previously known.*" Furthermore Stanton states in the last paragraph, that "Such demonstration can be beneficial, for example, for obtaining government regulatory approval for a new drug or a new use of a drug." Stanton actually teaches away from Applicant's required "essential" adverse event, since the term "essential" as defined by Applicant, implies a manufacture must disclose the adverse event information - as opposed to getting government approval (or approval from a regulatory agency) before disclosing the information - as taught by Stanton.

Accordingly, because Stanton requires a gene database (paragraph [0099]) as a critical element of the invention, which element is expressly excluded from Applicant's invention (paragraph [0103]), Stanton is not prior art to Applicant's invention. The Stanton database is not an "adverse event database" as described by Classen and does not mention a "novel *essential* adverse event." Thus, Stanton fails to teach each and every claim elements or limitations of Applicant's invention. To fill that deficiency, the Examiner has relied upon the Rivett abstract, but in Rivett there is no mention of creating a "database of proprietary essential adverse event data." While Rivett does mention a patent database, the claim limitation mentions a specific type of patent database. Thus, neither Stanton nor Rivett, alone or combined, suggest a database of "proprietary essential adverse events." Hence, even if combined, deficiencies remain, and at least one critical element of Applicant's invention cannot be provided by the cited prior art. Consequently, in accordance with patent law, if the cited prior art fails to teach each and every element of Applicant's invention, there can be no finding of obviousness of the cited claim. It is respectfully requested, therefore, that the rejection over ADPA, Stanton

and Rivette be reconsidered and withdrawn as a rejection of Applicant's claims under 35 U.S.C. §103(a).

Regarding ADPA, Stanton, Rivette and Colombo:

The Examiner has rejected Applicant's claims 251, 252, 254, 258 and 279 under 35 U.S.C. §103(a), as obvious and unpatentable over applicant disclosed prior art (ADPA) in view of Stanton (US Pub. No. 2002/0039990), and Rivette (US Pat. No. 5,991,751) in further view of Colombo (US Pat. No. 5,678,234). In making this rejection the Examiner relies upon ADPA, Stanton and Rivette for the reasons previously stated, and adds Colombo to disclose the value of commercialization.

For the above-stated reasons, ADPA, Stanton and Rivette fail to disclose , suggest or render Applicant's claim 250 or any claim dependent thereon obvious. As a result, simply adding knowledge of determining the value of commercializing a product still leaves one of ordinary skill in the art unable to determine an "essential" adverse event or to act with a method of use "responsive" to such a new essential adverse event. As such none of the cited references, including Colombo, alone or combined, suggest a database of "proprietary essential adverse events." Hence, even if combined, deficiencies remain, and at least one critical element of Applicant's invention cannot be provided by the cited prior art. Consequently, it is respectfully requested, therefore, that the rejection over ADPA, Stanton, Rivette and Colombo be reconsidered and withdrawn as a rejection of Applicant's claims under 35 U.S.C. §103(a).

Regarding ADPA, Stanton, Rivette, Colombo and Risen:

The Examiner has rejected Applicant's claim 258 over Leet, Rivette and Colombo. The Examiner has further rejected Applicant's claims 253 and 255 over ADPA, Stanton, Rivette, Colombo, and Risen (US Patent No. 6,018,714). In making this rejection the Examiner relies upon ADPA, Stanton, Rivette, and Colombo for the reasons previously stated, and adds Risen for the teaching of incorporating information into documents for selling, leasing or licensing the identified product information regarding a step of disclosing the value of commercialization. If the Examiner did intend to include Leet in this rejection, Applicant relies upon the arguments of record to demonstrate the limitations of Leet with regard to Applicant's invention.

For the above-stated reasons, ADPA, Stanton, Rivette and Colombo fail to disclose , suggest or render Applicant's claim 250 or any claim dependent thereon obvious. As a result, simply adding information into documents for selling, leasing or licensing the identified product information still leaves one of ordinary skill in the art unable to determine an "essential" adverse event or to act with a method of use "responsive" to such a new essential adverse event. As such none of the cited references, including Risen, alone or combined, suggest a database of "proprietary essential adverse events." Hence, even if combined, deficiencies remain, and at least one critical element of Applicant's invention cannot be provided by the cited prior art. Consequently, it is respectfully requested, therefore, that the rejection over ADPA, Stanton, Rivette, Colombo and Risen be reconsidered and withdrawn as a rejection of Applicant's claims under 35 U.S.C. §103(a).

Regarding ADPA, Stanton, Rivette, Colombo, Risen and Jacob:

The Examiner has rejected Applicant's claim 299 and 300 over ADPA, Stanton, Rivette, Colombo, Risen and Jacob (US Patent No. 3,885,566). In making this rejection the Examiner relies upon ADPA, Stanton, Rivette, Colombo and Risen for the reasons previously stated, and adds Jacob for teaching the printing of novel printed product safety information – specifically for disposable diapers.

For the above-stated reasons, ADPA, Stanton, Rivette, Colombo and Risen fail to disclose , suggest or render Applicant's claim 250 or any claim dependent thereon obvious. As a result, simply adding printing of novel printed product safety information to a product or device still leaves one of ordinary skill in the art unable to determine an "essential" adverse event or to act with a method of use "responsive" to such a new essential adverse event. As such none of the cited references, including Jacob, alone or combined, suggest a database of "proprietary essential adverse events." Hence, even if combined, deficiencies remain, and at least one critical element of Applicant's invention cannot be provided by the cited prior art. Consequently, it is respectfully requested, therefore, that the rejection over ADPA, Stanton, Rivette, Colombo, Risen and Jacob be reconsidered and withdrawn as a rejection of Applicant's claims under 35 U.S.C. §103(a).

It is respectfully submitted, therefore, that Applicant's pending claims are in condition for allowance, and Applicant respectfully requests that allowance be granted at the earliest date possible. Should the Examiner have any questions or comment regarding Applicant's amendments or response, the Examiner is asked to contact Applicants undersigned representative at (215) 772-7550.

If there are any fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-2424.

Respectfully submitted,

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Evelyn H. McConathy
Registration No. 35,279
Montgomery, McCracken, Walker & Rhoads, LLP
123 South Broad Street
Avenue of the Arts
Philadelphia, PA 19109
(215) 772-7550
(215)772-7620 (fax)